UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

1. **CERTIFICATE NUMBER:** 93-R-0464
CUSTOMER NUMBER: 15322

FORM APPROVED
OMB NO. 0579-0036

Western University Of Health Sciences
309 East Second Street
Pomona, CA 91766

(b)(6), (b)(7)c

Telephone: 909-469-5299

"A" by K. Garland 2/14/06

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, or experimentation, or held for these purposes. Attach additional sheets if necessary)

FACILITY LOCATIONS (Sites) - See Atached Listing

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY **(Attach additional sheets if necessarv or use APHIS Form 7023A)**

A. Animals Covered By The Animal Welfare Regulations	**B.** Number of animal being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not ye used for such purposes.	**C.** Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use o pain-relieving drugs.	**D.** Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals an for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	**E.** Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for wh the use of appropriate anesthetic, analgesic, or tranquiliz drugs would have adversely affected the procedures, res or interpretation of the teaching, research, experiments, surgery, or tests. (An explanation of the procedures producing pain or distress in these animals and the reasc such drugs were not used must be attached to this report	**F.** TOTAL NUMBER OF ANIMALS (COLUMNS C + D + E)
4. Dogs	0	0	0	0	0
5. Cats	0	0	0	0	0
6. Guinea Pigs	28	0	0	28	28
7. Hamsters	0	0	0	0	0
8. Rabbits	0	0	0	0	0
9. Non-human Primates	0	0	0	0	0
10. Sheep	0	0	0	0	0
11. Pigs	0	0	0	0	0
12. Other Farm Animals					
Chickens	0	12	0	0	~~0~~ 12
13. Other Animals					
Least shrews	194	0	0	50	50

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anestetic, analgesic, and tranquilizing drugs, prior to, during, and following actual rese teaching, testing, surgery, or experimentation were followed by this research facility.
2) Each principal investigator has considered alternatives to painful procedures.
3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and app Institutional Animal Care and Use Committee (IACUC). **A summary of all such exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary in brief explanation of the exceptions, as well as the species and number of animals affected.
4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
(Chief Executive Officer or Legally Responsible Institutional Official)

(b)(6), (b)(7)c

DATE SIGNED
11-22-05

NOV 25 2005

Column E Explanation

This form is intended as an aid to completing the Column E explanation. It is not an official form and its use is voluntary. Names, addresses, protocols, veterinary care programs, and the like, are not required as part of an explanation. A Column E explanation must be written so as to be understood by lay persons as well as scientists.

1. Registration Number: 93-R-0464 / 15322

2. Number 28 of animals used in this study.

3. Species (common name) Guinea pigs of animals used in the study.

4. Explain the procedure producing pain and/or distress.

   Guinea pigs are guillotined to obtain brain tissues, following the protocol recommended in the AVMA Policy on Euthaniaia (2000).

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)

   A review of the pharmacology of currently available anesthetics indicates that anesthetics elevate prolactin levels (as well as other pituitary hormones) by a direct action on the hypothalamic A12 dopamine neurons that tonically inhibit prolactin release. The release of prolactin adversely affects the electrophysiological records of hypothalamic slices being studied in the protocol. Review of the current literature of acceptable means of euthanization conducted by the PI and reviewed by the IACUC determined that all chemical means of euthanization would adversely impact the physiologic processes being investigated. Guillotining by appropriately trained personnel was determined to be the least painful means of euthanization available to meet the requirements of the study.

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

   Agency____________________ CFR____________________

DEC - 5 2005

Column E Explanation

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1. Registration Number: 93-R-0464 / 15322

2. Number 50 of animals used in this study.

3. Species (common name) Least shrews of animals used in the study.

4. Explain the procedure producing pain and/or distress.

   Numerous studies have shown that administration of anesthetics and/or analgesics can alter neurotransmitter release, their signal transduction mechanisms as well as their receptor number. Since several of these receptors are involved in my studies, administration of such agents prior sacrifice will alter the attained results. In addition, drug/drug interactions can also result which will compound the interpretation of the attained results [e.g. Dahmani, S. et al. (2004) Effects of anesthetic agents on focal adhesion kinase (pp125fak) tyrosine phosphorylation in rat hippocampal slices. Anesthesiology 101:344-353; Sandstrom DJ (2004 Isoflurane depresses glutamate release by reducing neuronal excitability at the drosophila neuromuscular junction. J. Physiol 558:489-502; Stiller CO et al. (2003) Microdialysis in pain research. Adv Drug Deliv Rev. 55:1065-1079; Pashkov VN et al. (2002) The effects of anesthetics on norepinephrine release from isolated rat cortical nerve terminals. Anesth Analag 96:1274-1281; etc]

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)

   Emesis studies; the least shrew is the best animal model of emesis for the proposed studies. I cannot imagine it will be feasible to use such large numbers of cats or dogs. The head-twitch response (HTR), ear-scratch response (ESR) and the serotonin syndrome are the most widely used behavioral paradigms for serotonergic drugs. Rats are more sensitive to serotonergic drugs that induce the serotonin syndrome whereas mice exhibit good frequencies of head-twitches to serotonergics(Darmani, N.A. and Ahmad, B. (2000) Early postnatal cocaine exposure in mice causes sequential, dose-dependent, enduring but reversible supersensitivity in 5-HT2A receptor-mediated function during development. Neurotoxicol. Teratol. 22:61-69; Darmani, N.A. and Ahmbad, B. (1999) Long term sequential determination of behavioral ontogeny of 5-HT1A- and 5-HT2-receptor functions in the rat. J. Pharmacol. Exp. Therap. 288:247-253.) More recently, we have found that shrews are even more sensitive and can separate the effects of some 5-HT antagonists which the mice and rats are unable to differentiate between them (Darmani, N.A. and Zhao, W. (1998) Production of serotonin syndrome by 8-OH DPAT in Cryptotis parva. Physiol. Behav. 65:327-331;Darmani, N.A., Mock, O., Towns, L. and Gerdes, C. (1994) The head-twitch response in the least shrew (Cryptotis parva) is a 5-HT2- and not a 5-HT1C-mediated phenomenon. Pharmacol. Biochem. Behav. 48:383-396.). This will greatly enhance the research in this field since elective antagonists for 5-HT 2C- and 5-HT2A- receptors do not exist.

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

   Agency__________ CFR__________

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